Human DAZL, DAZ and BOULE genes modulate primordial germ-cell and haploid gamete formation.

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Public Summary:
This manuscript was the first to report the use of human embryonic stem cells to probe the genetics of human germ cell formation and differentiation. The manuscript examined overexpression and silencing of genes on the human Y chromosome and autosomes. We found that these genes control germ cell numbers and differentiation. This allows us to understand how development is controlled especially key decisions.

Scientific Abstract:
The leading cause of infertility in men and women is quantitative and qualitative defects in human germ-cell (oocyte and sperm) development. Yet, it has not been possible to examine the unique developmental genetics of human germ-cell formation and differentiation owing to inaccessibility of germ cells during fetal development. Although several studies have shown that germ cells can be differentiated from mouse and human embryonic stem cells, human germ cells differentiated in these studies generally did not develop beyond the earliest stages. Here we used a germ-cell reporter to quantify and isolate primordial germ cells derived from both male and female human embryonic stem cells. By silencing and overexpressing genes that encode germ-cell-specific cytoplasmic RNA-binding proteins (not transcription factors), we modulated human germ-cell formation and developmental progression. We observed that human DAZL (deleted in azoospermia-like) functions in primordial germ-cell formation, whereas closely related genes DAZ and BOULE (also called BOLL) promote later stages of meiosis and development of haploid gametes. These results are significant to the generation of gametes for future basic science and potential clinical applications.